

**In Claims:**

1. (Original) A composition for inhibiting the pathological activities of matrix metalloproteinases comprising an effective amount of NNN'N'-Tetrakis- (2-pyridyl-methyl)-ethylenediamine, (TPEN) and a pharmaceutically acceptable carrier.

2. (Original) A composition for inhibiting the pathological activities of matrix metalloproteinases as in claim 1, wherein the TPEN is in a concentration of 0.001-100 micromolar.

3. (Original) A composition for inhibiting the pathological activities of matrix metalloproteinases as in claim 1, where the active substance is a derivative, metal complexes and other forms of complexes of TPEN, including but not limited to ethylenediamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanol amine, aminoethylpiperazine, pentaethylenehexamine, triethylenetetramine-hydrochloride, tetraethylenepentamine-hydrochloride, pentaethylenehexamine-hydrochloride, tetraethylpentamine, captopril, penicilamine and transition metal binding peptides, wherein the composition is in concentration, but not limited to, of 0.001-100 micromolar.

4. (Original) A use of TPEN for the manufacture of a pharmaceutical composition for the treatment or prevention of pathological conditions influenced by the action of matrix metalloproteinases (MMPs).

5. (Currently amended) The use, according to ~~claims 3 and 4~~ claim 3, wherein the disease influenced by the action of MMPs is atherosclerosis, corneal ulceration, emphysema, asthma, osteoarthritis, chondrolitis and chondrosarcoma, osteoporosis, rheumatoid arthritis and other inflammatory disorders, autoimmune diseases, ulcerative colitis, primary malignancy, various types of carcinoma hodgkin's disease, various lymphomas and other hematological diseases, tumor invasion metastasis, angiogenesis and vasculogenesis, ischemia-reperfusion injury, stroke, acute MI, coronary artery diseases and thrombolysis-associated hemorrhagic transformation, neurodegenerative diseases, Alzheimer's disease, Multiple Sclerosis, glaucoma, cataract and optic-nerve trauma, brain-trauma, vascular thrombolysis and restenosis, aortic and blood vessels aneurism, types of vasculitis as Kawasaki disease, ischemic heart and lung diseases, apoptosis, diabetes, digestive system disorders, organ rejection, infectious diseases, and mucosal pathogens such as N gonorrhoeae, P. gingivalis and other periodontal diseases, and sepsis, chronic wound and granulomas.

6.. (Currently amended) The use, according to ~~any of the preceding claims~~ claim 1, wherein the pharmaceutical composition is formulated for oral, parenteral or intradermal administration.

7. (Currently amended) The use according to ~~any of the claims 1 to 6~~ claim 1, wherein the pharmaceutical composition is formulated as a single pharmaceutical composition.

8. (Original) A composition for inhibiting the pathological activities of matrix metalloproteinases as in claim 1, wherein the TPEN is in the form of a metal complex formed with a metal.

9. (Original) A composition according to claim 8, wherein the metal is an inert metal.

10. (Original) A composition according to claim 8, wherein the metal complex is also for use in scavenging free radicals.

11. (Original) A use of TPEN as an anti-angiogenic agent in a pharmaceutical composition.

12. (Original) A use of TPEN as an anti-metastatic agent in a pharmaceutical composition.

13. (Original) A use of TPEN as an anthrax-anti toxin.

14. (Original) A use of TPEN for inhibiting the spread of cancer in organs, cells, and tissue of the body.

15. (Original) A use of TPEN for the inhibition or prevention of ischemia and reperfusion injury in organs, cells, and tissues of the body where MMP activity plays a role.

16. (Original) A composition for inhibiting the pathological activities of matrix metalloproteinases comprising an effective amount of a highly specific metal chelator and a pharmaceutically acceptable carrier.

17. (Original) The composition, according to claim 16, wherein the metal chelator is a high affinity  $\text{Zn}^{2+}$  or  $\text{Cu}^{2+}$  polyamine chelating agent.

18. (Original) The composition, according to claim 17, wherein the polyamine chelating agent is selected from the group consisting of ethylenediamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanol amine, aminoethylpiperazine, pentaethylenhexamine, triethylenetetramine-hydrochloride, tetraethylenepentamine-hydrochloride, pentaethylenhexamine-hydrochloride, tetraethylpentamine, captopril, penicilamine and transition metal binding peptides.

19. (Original) A method for inhibiting metalloprotease activity comprising administering a pharmaceutical agent adapted for depriving metalloproteases of essential metal ions.

20. (Original) A method of treating a subject having a pathological condition influenced by the action of MMP, comprising administering to the subject an amount of TPEN or any one of its derivatives effective to treat or prevent the pathological condition.

21. (Original) A method according to claim 20, wherein the pathological condition influenced by the action of MMP is selected from the group consisting of: atherosclerosis, corneal ulceration, emphysema, asthma, osteoarthritis, chondrolitis and chondrosarcoma, osteoporosis, rheumatoid arthritis and other inflammatory disorders, autoimmune diseases, ulcerative colitis, primary malignancy, various types of carcinoma, Hodgkin's disease, various lymphomas and other hematological diseases, tumor invasion, metastasis, angiogenesis and vasculogenesis, ischemia-reperfusion injury, stroke, acute MI, coronary artery diseases and thrombolysis-associated hemorrhagic transformation, neurodegenerative diseases, Alzheimer's disease, Multiple Sclerosis, glaucoma, cataract and optic-nerve trauma, brain-trauma, vascular thrombolysis and restenosis, aortic and blood vessels aneurism, types of vasculitis as Kawasaki disease, ischemic heart and lung diseases, apoptosis, diabetes, digestive system disorders, organ rejection, infectious diseases, and mucosal pathogens such as *N. gonorrhoeae*, *P. gingivalis* and other periodontal diseases, and sepsis, chronic wound and granulomas.

22. (Original) A method according to claim 21, wherein the generation and/or action of MMP is induced and/or influenced by Nitros-Oxide (NO) and/or free radicals..

23. (Original) A method of treating a subject having or suspected of having a pathological condition influenced by the action of Cyclooxygenases, endonucleases, Metalloproteinases and 5-lipoxygenase comprising administering to the subject an amount of TPEN effective to inhibit the action of MMP.

24. (Original) A method according to claim 22, wherein the cyclooxygenase is COX-1 or COX-2.

25. (Original) A method for treating a subject having a pathological condition for which the presence of a metal ion is required, comprising administering a metal ion chelator to the subject.

26. (Original) A method of treating a subject having or suspected of having a pathological condition influenced by the action of MMP, Cyclooxygenases, endonucleases, Metalloproteinases and 5-lipoxygenase comprising administering to the subject an amount of TPEN-Germanium complex, or organic or inorganic Germanium alone, effective to inhibit the action of MMP.

27. (Currently amended) A method according to claim 25, wherein the pathological condition influenced by the action of MMP is selected from the group of pathological conditions ~~expressed in claim 21~~ consisting of: atherosclerosis, corneal ulceration, emphysema, asthma, osteoarthritis, chondrolitis and chondrosarcoma, osteoporosis, rheumatoid arthritis and other inflammatory disorders, autoimmune diseases, ulcerative colitis, primary malignancy, various types of carcinoma hodgkin's disease, various lymphomas and other hematological diseases, tumor invasion metastasis, angiogenesis and vasculogenesis, ischemia-reperfusion injury, stroke, acute MI, coronary artery diseases and thrombolysis-associated hemorrhagic transformation, neurodegenerative diseases, Alzheimer's disease, Multiple Sclerosis, glaucoma, cataract and optic-nerve trama, brain-trauma, vascular thrombolysis and restenosis, aortic and blood vessels aneurism, types of vasculitis as Kawasaki disease, ischemic heart and lung diseases, apoptosis, diabetes, digestive system disorders, organ rejection, infectious diseases, and mucosal pathogens such as N gonorrhoeae, P.gingivalis and other periodontal diseases, and sepsis, chronic wound and granulomas..

\_\_\_\_ 28. (Currently amended) A method according to ~~claims 25 and 26~~ claim 25, wherein the Germanium is in complex with a polyamine chelating agent selected from the ~~group of agents according to claim 18~~ consisting of ethylenediamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenep entamine, aminoethylethanol amine, aminoethylpiperazine,

pentaethylenhexamine, triethylenetetramine-hydrochloride,  
tetraethylenepentamine-hydrochloride, pentaethylenhexamine-hydrochloride,  
tetraethylpentamine, captopril, penicilamine and transition metal binding  
peptides..

29. (Original) A method for inhibiting the lethal factor produced by toxigenic strains of anthrax bacteria comprising exposing said lethal factor to an efficient amount of a highly specific zinc chelator.

30. (Original) A method for inhibiting activities of fungi, bacteria, or plants that utilize zinc-dependent methionine synthetase (MetE) comprising delivering to an organism utilizing zinc-dependent methionine synthetase for metabolic activities an efficient amount of a highly specific zinc chelator.

31. (Original) A method for inhibiting the activity of a zinc-dependent enzyme in prokaryotic systems, comprising exposing a zinc-dependent enzyme to an efficient amount of a highly specific zinc chelator.

32. (Original) A method for inhibiting the activity of a zinc-dependent enzymes, wherein the enzymes are specifically beta-lactamases.

33. (Original) A method according to claim 30, wherein the chelator is TPEN or a TPEN derivative.